

FEB 20 2007

Application No.: 10/705,389

Docket No.: 070702009320

REMARKS

The Examiner has rejected claims 1, 4-20, 22, and 23 under 35 USC 112, second paragraph, as lacking enablement.

First, the Examiner states that the claims encompass the sequencing of any nucleic acid, no matter how long or complex. In addition, the Examiner states that the quantity of experimentation necessary for enabling the full scope of the claimed invention is vast given that the claimed method fairly encompasses the simultaneous sequencing of any number and combination of nucleic acids. Independent claims 1 and 15 have been amended, and the claims as amended now involve the sequencing of single-stranded nucleic acids. The method of synthesizing a double-stranded molecule from a single-stranded molecule was well known to those skilled in the art to which the application pertains at the time of filing. As for the number and combination of nucleic acids to sequence, it is well within the ability and discretion of those skilled in the art to determine the appropriate number of nucleic acids to sequence in accordance with the claimed method to obtain the optimal result. Accordingly, Applicants respectfully request the withdrawal of this rejection.

Secondly, the Examiner states that Doucette-Stamm *et al.* (US Patent 7,129,340) teaches that specificity issues result when using primers greater than 100 nucleotides in length and yet the claimed method does not specify the length of the primer. Doucette-Stamm concerns the length of primers, not the length of the template nucleic acid. Applicants are not claiming any specific primer but rather a method for sequencing a nucleic acid. It was well within the ability of those skilled in the art to select a suitable primer to start a sequencing reaction rather than look for a primer that does not work. Since the selection of suitable primer was well within the ability of those skilled in biotechnology at the time the application was filed, undue experimentation was not involved. Accordingly, Applicants respectfully request the withdrawal of this rejection.

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Thirdly, the Examiner states that the claimed method fairly encompasses the use of virtually any polymerase, including Klenow fragment which may have several limitations according to Burns (US Patent 7,066,453 B2). Applicants are not claiming any specific polymerase but rather a method for sequencing a nucleic acid. While Applicants do not comment on the suitability of Klenow fragments as a polymerase for the claimed embodiments, Klenow fragment is only one specific type of polymerase and there are many other polymerases which are suitable for DNA sequencing. It was well within the ability of those skilled in the art to select a suitable polymerase to start the sequencing reaction rather than look for a polymerase that does not work well. Since undue experimentation was not involved in selecting a polymerase that works, Applicants respectfully request the withdrawal of this rejection.

Fourthly, the Examiner states that Cheeseman (Patent Number 5,302,509) teaches using a 3'-O-blocking group that blocks the continuous incorporation of nucleotides to the template nucleic acid and that the claimed method would not function because the claimed method depend upon the monitoring of the very incorporation of nucleotides by a polymerase. Cheeseman purposefully utilizes the blocking group to temporarily hold the incorporation of nucleotides. There are many labeling groups which allow the continuous incorporation of nucleotides, and those skilled in the art need not use a blocking group as a label if the continuous incorporation of nucleotide is desired. Applicants respectfully request the withdrawal of this rejection.

Claims 1, 4-20, 22, and 23 are rejected under 35 USC 103(a) over Allen in view of Lee and further in view of Quate. Specifically, the Examiner states that:

Allen discloses a method of sequencing nucleic acids where an atomic force microscope cantilever is used. * * * Lee et al., disclose a method of characterizing a nucleic acid wherein the nucleic acid is attached to the surface of a cantilever. * * * Quate et al., teach in greater detail of the binding of molecules to the surface of a cantilever and the detection of molecular interactions.

In view of the detailed teachings of the prior art, the ordinary artisan would have had a most reasonable expectation of success, and would have been amply motivated as the method would achieve the same result, sequencing of a nucleic acid, but do so in a more direct

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manner by having the molecules of interest being attached to the cantilever, and therein requiring less steps and manipulation.

The alleged reason to combine the references stated above is not sufficient to make out a prima facie case of obviousness because the motivation did not come from a prior art, but from applicants' disclosure which provides a roadmap to the claimed invention. Accordingly, the Examiner is impermissibly using hindsight to arrive at the claimed invention. Specifically, as explained in the previous Response, the AFM cantilever disclosed in Allen operates in a much different fashion from the cantilevers disclosed in the claimed embodiments. Neither Allen nor any of the other references cited by the Examiner provide any motivation to substitute the AFM cantilever utilized in Allen for the claimed cantilever. Accordingly, one of ordinary skill in the art would not arrive at the claimed invention as suggested by the Examiner. Since there is no motivation to combine Allen with Lee and Quate, Applicants respectfully request that this rejection be withdrawn.

In view of the above, each of the presently pending claims in this application is in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and

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authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **070702009320**.

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Respectfully submitted,

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